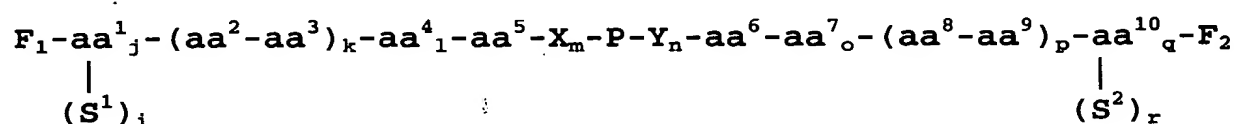


1. The composition of claim 1, comprising an amino acid sequence selected from the group consisting of KDPJGYVHDAPVGJPKG<sub>Y</sub> (SEQ ID NO:212), KDPJGYVHDAPVPKG<sub>Y</sub> (SEQ ID NO:213), and KDPYVHDAPVGJPKG<sub>Y</sub> (SEQ ID NO:214).

2. The composition of claim 1, comprising the amino acid sequence - KDBJGSEVNLDAEFGJPKDDY (SEQ ID NO:215).

3. A fluorogenic composition for the detection of the activity of a protease, said composition having the formula:



wherein

P is a peptide selected from the group consisting YVHDAPV (SEQ ID NO:[212]216), and dYVHDAPV (SEQ ID NO:[213]217);

F<sup>1</sup> and F<sup>2</sup> are fluorophores and F<sup>1</sup> is attached to the amino terminal amino acid and F<sup>2</sup> is attached to the carboxyl terminal amino acid;

S<sup>1</sup> and S<sup>2</sup>, when present, are peptide spacers ranging in length from 1 to about 50 amino acids and S<sup>1</sup>, when present, is attached to the amino terminal amino acid and S<sup>2</sup>, when present, is attached to the carboxyl terminal amino acid;

i, j, k, l, m, n, o, p, q, and r are independently 0 or 1;

aa<sup>1</sup> and aa<sup>10</sup> are independently selected from the group consisting of lysine, ornithine and cysteine;

aa<sup>2</sup>, aa<sup>3</sup>, aa<sup>8</sup>, and aa<sup>9</sup> are independently selected from the group consisting of an amino acid or a dipeptide consisting of Asp, Glu, Lys, Ornithine, Arg, Citulline, homocitrulline, Ser, homoserine, Thr, and Tyr;

aa<sup>5</sup>, aa<sup>4</sup>, aa<sup>6</sup>, and aa<sup>7</sup> are independently selected from the group consisting of proline, 3,4-dehydropoline, hydroxyproline, alpha aminoisobutyric acid and N-methyl alanine;

X is selected from the group consisting of Gly, βAla, γAbu, Gly-Gly, Ahx, βAla-Gly, βAla-βAla, γAbu-Gly, βAla-γAbu, Gly-Gly-Gly, γAbu-γAbu, Ahx-Gly, βAla-Gly-Gly, Ahx-βAla,

$\beta$ Ala- $\beta$ Ala-Gly, Gly-Gly-Gly-Gly, Ahx- $\gamma$ Abu,  $\beta$ Ala- $\beta$ Ala- $\beta$ Ala,  $\gamma$ Abu- $\beta$ Ala-Gly,  $\gamma$ Abu- $\gamma$ Abu-Gly, Ahx-Ahx,  $\gamma$ Abu- $\gamma$ Abu- $\beta$ Ala, and Ahx-Ahx-Gly;

Y is selected from the group consisting of Gly,  $\beta$ Ala,  $\gamma$ Abu, Gly-Gly, Ahx, Gly- $\beta$ Ala,  $\beta$ Ala- $\beta$ Ala, Gly- $\gamma$ Abu,  $\gamma$ Abu- $\beta$ Ala, Gly-Gly-Gly,  $\gamma$ Abu- $\gamma$ Abu, Gly-Ahx, Gly-Gly- $\beta$ Ala,  $\beta$ Ala-Ahx, Gly- $\beta$ Ala- $\beta$ Ala, Gly-Gly-Gly-Gly (SEQ ID NO:[214]211),  $\gamma$ Abu-Ahx,  $\beta$ Ala- $\beta$ Ala- $\beta$ Ala, Gly- $\beta$ Ala- $\gamma$ Abu, Gly- $\gamma$ Abu- $\gamma$ Abu, Ahx-Ahx,  $\beta$ Ala- $\gamma$ Abu- $\gamma$ Abu, and Gly-Ahx-Ahx; and

when i is 1, S<sup>1</sup> is joined to aa<sup>1</sup> by a peptide bond through a terminal alpha amino group of aa<sup>1</sup>; and when r is 1, S<sup>2</sup> is joined to aa<sup>10</sup> by a peptide bond through a terminal alpha carboxyl group of aa<sup>10</sup>.

4. The composition of claim 21, comprising an amino acid sequence selected from the group consisting of KDBYVHDAPVPGKY (SEQ ID NO:[215]218), KDBGYVHDAPVGPKGY (SEQ ID NO:[216]219), KDBJGYVHDAPVGJPKGY (SEQ ID NO:[217]220), and KDBJGdYVHDAPVGJPKGY (SEQ ID NO:[218]221).

These amendments are made without prejudice and are not to be construed as abandonment of the previously claimed subject matter or agreement with the Examiner's position. In accordance with the requirements of 37 C.F.R. § 1.121, a marked up version showing the changes to the claims, is attached herewith as Appendix A.

#### REMARKS

The Notice of Missing Parts indicated that the application is not in compliance with sequence rules, 37 C.F.R. §§ 1.821-1.825. A disk containing the referenced sequence(s) in computer readable form, and a paper copy of the sequence information that has been printed from the floppy disk are provided herewith. The information contained in the computer readable disk was prepared through the use of the software program "PatentIn" and is identical to that of the paper copy. The sequence listing introduces no new matter and simply contains sequences found within the application as filed.

If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (510) 337-7871.

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Respectfully submitted,



Tom Hunter  
Reg. No: 38,498

**APPENDIX A****VERSION WITH MARKINGS TO SHOW CHANGES MADE IN 09/874,350 WITH ENTRY OF THIS AMENDMENT****In the specification:**

Page 25, lines 13-26:

In a particularly preferred embodiment, aa<sup>1</sup> and aa<sup>10</sup> are independently selected from the group consisting of lysine, ornithine and cysteine; aa<sup>2</sup>, aa<sup>3</sup>, aa<sup>8</sup> and aa<sup>9</sup> are independently selected from the group consisting of an amino acid or a dipeptide consisting of Asp, Glu, Lys, Ornithine, Arg, Citulline, homocitrulline, Ser, homoserine, Thr, and Tyr; aa<sup>5</sup>, aa<sup>4</sup>, aa<sup>6</sup>, and aa<sup>7</sup> are independently selected from the group consisting of proline, 3,4-dehydropyrrolidine, hydroxyproline, alpha aminoisobutyric acid and N-methyl alanine; X is selected from the group consisting of Gly,  $\beta$ Ala,  $\gamma$ Abu, Gly-Gly, Ahx,  $\beta$ Ala-Gly,  $\beta$ Ala- $\beta$ Ala,  $\gamma$ Abu-Gly,  $\beta$ Ala- $\gamma$ Abu, Gly-Gly-Gly,  $\gamma$ Abu- $\gamma$ Abu, Ahx-Gly,  $\beta$ Ala-Gly-Gly, Ahx- $\beta$ Ala,  $\beta$ Ala- $\beta$ Ala-Gly, Gly-Gly-Gly-Gly, Ahx- $\gamma$ Abu,  $\beta$ Ala- $\beta$ Ala- $\beta$ Ala,  $\gamma$ Abu- $\beta$ Ala-Gly,  $\gamma$ Abu- $\gamma$ Abu-Gly, Ahx-Ahx,  $\gamma$ Abu- $\gamma$ Abu- $\beta$ Ala, and Ahx-Ahx-Gly; Y is selected from the group consisting of Gly,  $\beta$ Ala,  $\gamma$ Abu, Gly-Gly, Ahx, Gly- $\beta$ Ala,  $\beta$ Ala- $\beta$ Ala, Gly- $\gamma$ Abu,  $\gamma$ Abu- $\beta$ Ala, Gly-Gly-Gly,  $\gamma$ Abu- $\gamma$ Abu, Gly-Ahx, Gly-Gly- $\beta$ Ala,  $\beta$ Ala-Ahx, Gly- $\beta$ Ala- $\beta$ Ala, Gly-Gly-Gly-Gly (SEQ ID NO: [2]211),  $\gamma$ Abu-Ahx,  $\beta$ Ala- $\beta$ Ala- $\beta$ Ala, Gly- $\beta$ Ala- $\gamma$ Abu, Gly- $\gamma$ Abu- $\gamma$ Abu, Ahx-Ahx,  $\beta$ Ala- $\gamma$ Abu- $\gamma$ Abu, and Gly-Ahx-Ahx.

Page 61, lines 17-27:

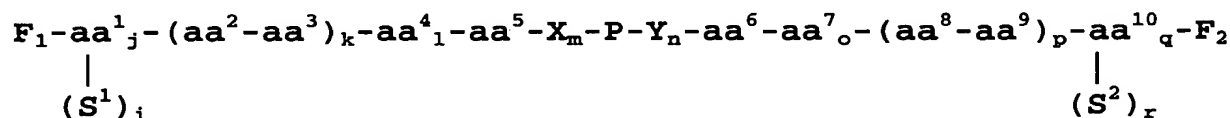
--The elastase substrate, Fm-K[F1]DAIPNluSIPK[F1]GY (SEQ ID NO:185), (where F1 was carboxytetramethylrhodamine, Fm was Fmoc, K[F1] was F1 covalently attached through the epsilon amino group of lysine (K), and Fm-K is the Fmoc group covalently attached at the alpha amino group of the amino terminal lysine residue) was used with HL-60 cells. Cells were incubated with various concentrations of elastase substrate ranging from 10 nM to 10  $\mu$ M for 5 minutes to 60 minutes. Then the cells were diluted 5-fold with RPMI 1640 medium containing 5% serum or with phosphate buffered saline. The samples were centrifuged and washed once more with 1 ml of washing solution. After centrifugation and removal of the washing solution, cell pellets were loosened with about 25  $\mu$ l of medium and these cells were transferred to a glass capillary. Capillary tubes were then placed on a glass microscope slide and examined under a fluorescence microscope using standard rhodamine filters.

**In the claims:**

5. The composition of claim 1, comprising an amino acid sequence selected from the group consisting of KDPJGYVHDAPVGJPKG<sub>Y</sub> (SEQ ID NO:212), KDPJGYVHDAPVPKG<sub>Y</sub> (SEQ ID NO:213), and KDPYVHDAPVGJPKG<sub>Y</sub> (SEQ ID NO:214).

6. The composition of claim 1, comprising the amino acid sequence - KDBJGSEVNLD<sub>A</sub>EF<sub>G</sub>JP<sub>K</sub>DD<sub>Y</sub> (SEQ ID NO:215).

7. A fluorogenic composition for the detection of the activity of a protease, said composition having the formula:



wherein

P is a peptide selected from the group consisting YVHDAPV (SEQ ID NO:[212]216), and dYVHDAPV (SEQ ID NO:[213]217);

F<sup>1</sup> and F<sup>2</sup> are fluorophores and F<sup>1</sup> is attached to the amino terminal amino acid and F<sup>2</sup> is attached to the carboxyl terminal amino acid;

S<sup>1</sup> and S<sup>2</sup>, when present, are peptide spacers ranging in length from 1 to about 50 amino acids and S<sup>1</sup>, when present, is attached to the amino terminal amino acid and S<sup>2</sup>, when present, is attached to the carboxyl terminal amino acid;

i, j, k, l, m, n, o, p, q, and r are independently 0 or 1;

aa<sup>1</sup> and aa<sup>10</sup> are independently selected from the group consisting of lysine, ornithine and cysteine;

aa<sup>2</sup>, aa<sup>3</sup>, aa<sup>8</sup>, and aa<sup>9</sup> are independently selected from the group consisting of an amino acid or a dipeptide consisting of Asp, Glu, Lys, Ornithine, Arg, Citulline, homocitrulline, Ser, homoserine, Thr, and Tyr;

aa<sup>5</sup>, aa<sup>4</sup>, aa<sup>6</sup>, and aa<sup>7</sup> are independently selected from the group consisting of proline, 3,4-dehydroproline, hydroxyproline, alpha aminoisobutyric acid and N-methyl alanine;

X is selected from the group consisting of Gly,  $\beta$ Ala,  $\gamma$ Abu, Gly-Gly, Ahx,  $\beta$ Ala-Gly,  $\beta$ Ala- $\beta$ Ala,  $\gamma$ Abu-Gly,  $\beta$ Ala- $\gamma$ Abu, Gly-Gly-Gly,  $\gamma$ Abu- $\gamma$ Abu, Ahx-Gly,  $\beta$ Ala-Gly-Gly, Ahx- $\beta$ Ala,  $\beta$ Ala- $\beta$ Ala-Gly, Gly-Gly-Gly-Gly, Ahx- $\gamma$ Abu,  $\beta$ Ala- $\beta$ Ala- $\beta$ Ala,  $\gamma$ Abu- $\beta$ Ala-Gly,  $\gamma$ Abu- $\gamma$ Abu-Gly, Ahx-Ahx,  $\gamma$ Abu- $\gamma$ Abu- $\beta$ Ala, and Ahx-Ahx-Gly;

Y is selected from the group consisting of Gly,  $\beta$ Ala,  $\gamma$ Abu, Gly-Gly, Ahx, Gly- $\beta$ Ala,  $\beta$ Ala- $\beta$ Ala, Gly- $\gamma$ Abu,  $\gamma$ Abu- $\beta$ Ala, Gly-Gly-Gly,  $\gamma$ Abu- $\gamma$ Abu, Gly-Ahx, Gly-Gly- $\beta$ Ala,  $\beta$ Ala-Ahx, Gly- $\beta$ Ala- $\beta$ Ala, Gly-Gly-Gly-Gly (SEQ ID NO:[214]211),  $\gamma$ Abu-Ahx,  $\beta$ Ala- $\beta$ Ala- $\beta$ Ala, Gly- $\beta$ Ala- $\gamma$ Abu, Gly- $\gamma$ Abu- $\gamma$ Abu, Ahx-Ahx,  $\beta$ Ala- $\gamma$ Abu- $\gamma$ Abu, and Gly-Ahx-Ahx; and

when i is 1,  $S^1$  is joined to  $aa^1$  by a peptide bond through a terminal alpha amino group of  $aa^1$ ; and when r is 1,  $S^2$  is joined to  $aa^{10}$  by a peptide bond through a terminal alpha carboxyl group of  $aa^{10}$ .

8. The composition of claim 21, comprising an amino acid sequence selected from the group consisting of KDBYVHDAPVPKG<sub>Y</sub> (SEQ ID NO:[215]218), KDBGYVHDAPVGPKG<sub>Y</sub> (SEQ ID NO:[216]219), KDBJGYVHDAPVGJPKG<sub>Y</sub> (SEQ ID NO:[217]220), and KDBJGdYVHDAPVGJPKG<sub>Y</sub> (SEQ ID NO:[218]221).